

SEQUENCE LISTING

<110> Langenfeld, John
 <120> BONE MORPHOGENETIC PROTEIN-2 IN THE TREATMENT AND DIAGNOSIS OF
 CANCER
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 <150> US60/261,252
 <151> 2001-01-12
 <150> US10/044,716
 <151> 2002-01-11
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<223> TGFB; Region: Transforming growth factor-beta (TGF-beta) family

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ctgcggtctc ctaaagggtcg acc atg gtg gcc ggg acc cgc tgt ctt cta gcg      353
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Leu Leu Leu Pro Gln Val Leu Leu Gly Gly Ala Ala Gly Leu Val Pro
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gag ctg ggc cgc agg aag ttc gcg gcg gcg tcg tcg ggc cgc ccc tca      449
Glu Leu Gly Arg Arg Lys Phe Ala Ala Ala Ser Ser Gly Arg Pro Ser
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tcc cag ccc tct gac gag gtc ctg agc gag ttc gag ttg cgg ctg ctc      497
Ser Gln Pro Ser Asp Glu Val Leu Ser Glu Phe Glu Leu Arg Leu Leu
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agc atg ttc ggc ctg aaa cag aga ccc acc ccc agc agg gac gcc gtg      545
Ser Met Phe Gly Leu Lys Gln Arg Pro Thr Pro Ser Arg Asp Ala Val
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Val Pro Pro Tyr Met Leu Asp Leu Tyr Arg Arg His Ser Gly Gln Pro
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ggc tca ccc gcc cca gac cac cgg ttg gag agg gca gcc agc cga gcc      641
Gly Ser Pro Ala Pro Asp His Arg Leu Glu Arg Ala Ala Ser Arg Ala
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aac act gtg cgc agc ttc cac cat gaa gaa tct ttg gaa gaa cta cca      689
Asn Thr Val Arg Ser Phe His His Glu Glu Ser Leu Glu Glu Leu Pro
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Ile Asn Ile Tyr Glu Ile Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe			
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ccc gtg acc aga ctt ttg gac acc agg ttg gtg aat cag aat gca agc			929
Pro Val Thr Arg Leu Leu Asp Thr Arg Leu Val Asn Gln Asn Ala Ser			
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Arg Trp Glu Ser Phe Asp Val Thr Pro Ala Val Met Arg Trp Thr Ala			
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Gln Gly His Ala Asn His Gly Phe Val Val Glu Val Ala His Leu Glu			
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His Pro Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp Trp Ile			
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Val Ala Pro Pro Gly Tyr His Ala Phe Tyr Cys His Gly Glu Cys Pro			
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Val Leu Ser Glu Phe Glu Leu Arg Leu Leu Ser Met Phe Gly Leu Lys
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Gln Arg Pro Thr Pro Ser Arg Asp Ala Val Val Pro Pro Tyr Met Leu
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Asp Leu Tyr Arg Arg His Ser Gly Gln Pro Gly Ser Pro Ala Pro Asp
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His His Glu Glu Ser Leu Glu Glu Leu Pro Glu Thr Ser Gly Lys Thr
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Thr Arg Arg Phe Phe Phe Asn Leu Ser Ser Ile Pro Thr Glu Glu Phe
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Leu Gly Asn Asn Ser Ser Phe His His Arg Ile Asn Ile Tyr Glu Ile
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Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe Pro Val Thr Arg Leu Leu
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Asp Thr Arg Leu Val Asn Gln Asn Ala Ser Arg Trp Glu Ser Phe Asp
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Val Thr Pro Ala Val Met Arg Trp Thr Ala Gln Gly His Ala Asn His
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Gly Phe Val Val Glu Val Ala His Leu Glu Glu Lys Gln Gly Val Ser
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Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His Lys Gln
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His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His
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Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala
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<301> Valenzuela,D.M., Economides,A.N., Rojas,E., Lamb,T.M., Nunez,L.,
 Jones,P., Ip,N.Y., Espinosa,R., Brannan,C.I., Gilbert,D.J.,
 Copeland,N.G., Jenkins,N.A., LeBeau,M.M., Harland,R.M. and
 Yancopoulos,G.D.

<302> Identification of mammalian noggin and its expression in the
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<303> J. Neurosci.

<304> 15

<305> 9

<306> 6077-6084

<307> 1995

<308> NM_005450

<309> 2000-11-01

<313> (1)..(699)

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<301> McMahon,J.A., Takada,S., Zimmerman,L.B., Fan,C.M., Harland,R.M.
 and McMahon, A.P.

<302> Noggin-mediated antagonism of BMP signaling is required for
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<303> Genes Dev.

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<307> 1998

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<301> Brunet,L.J., McMahon,J.A., McMahon,A.P. and Harland,R.M.

<302> Noggin, cartilage morphogenesis, and joint formation in the
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<303> Science

<304> 280

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<306> 1455-1457

<307> 1998

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<301> Smith, W.C.

<302> TGF beta inhibitors. New and unexpected requirements in
vertebrate development

<303> Trends Genet.

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Brunner,H.G., Reinker,K., Rimoin,D.L., Cohn,D.H., Goodman,F.R.,
Reardon,W., Patton,M., Francomano,C.A. and Warman,M.L.

<302> Heterozygous mutations in the gene encoding noggin affect human
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<303> Nat. Genet.

<304> 21

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<307> 1999

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His	Pro	Asp	Pro	Ile	Phe	Asp	Pro	Lys	Glu	Lys	Asp	Leu	Asn	Glu	Thr		
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ctg	ctg	cgc	tcg	ctg	ctc	ggg	ggc	cac	tac	gac	cca	ggc	ttc	atg	gcc	240	
Leu	Leu	Arg	Ser	Leu	Gly	Gly	His	Tyr	Asp	Pro	Gly	Phe	Met	Ala			
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Thr	Ser	Pro	Pro	Glu	Asp	Arg	Pro	Gly	Gly	Gly	Gly	Gly	Ala	Ala	Gly		
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Ser	Gly	Ala	Met	Pro	Ser	Glu	Ile	Lys	Gly	Leu	Glu	Phe	Ser	Glu	Gly		
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Ser	Cys	Phe	Ser	Lys	Arg	Ser	Cys	Ser	Val	Pro	Glu	Gly	Met	Val	Cys		
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aag	ccg	tcc	aag	tcc	gtg	cac	ctc	acg	gtg	ctg	cgg	tgg	cgc	tgt	cag	624	
Lys	Pro	Ser	Lys	Ser	Val	His	Leu	Thr	Val	Leu	Arg	Trp	Arg	Cys	Gln		
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Leu Leu Arg Ser Leu Leu Gly Gly His Tyr Asp Pro Gly Phe Met Ala
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Gly Ala Glu Asp Leu Ala Glu Leu Asp Gln Leu Leu Arg Gln Arg Pro
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Leu Ala Gln Gly Lys Lys Gln Arg Leu Ser Lys Lys Leu Arg Arg Lys
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Trp Asn Asp Leu Gly Ser Arg Phe Trp Pro Arg Tyr Val Lys Val Gly
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Leu Ala Gln Gly Lys Lys Gln Arg Leu Ser Lys Lys Leu Arg Arg Lys	
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 Francois, V.
 <302> The human chordin gene encodes several differentially expressed
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 <301> Millet, C., and Francois, V.

<302> Direct Submission
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 Met Pro Ser Leu Pro Ala Pro Pro Ala Pro Leu Leu Leu Leu
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 Gly Leu Leu Leu Leu Gly Ser Arg Pro Ala Arg Gly Ala Gly Pro Glu
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 Pro Pro Val Leu Pro Ile Arg Ser Glu Lys Glu Pro Leu Pro Val Arg
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Gly Ala Glu Glu Arg Ala Arg Gly Asp Gly His Thr Asp Phe Val Ala			
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20           25           30

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Ile Pro Pro Pro Asp Lys Ala Gln His Asn Asp Ser Glu Gln Thr Gln
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Ser Pro Gln Gln Pro Gly Ser Arg Asn Arg Gly Arg Gly Gln Gly Arg
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Gly Thr Ala Met Pro Gly Glu Glu Val Leu Glu Ser Ser Gln Glu Ala
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Leu His Val Thr Glu Arg Lys Tyr Leu Lys Arg Asp Trp Cys Lys Thr
 85 90 95

Gln Pro Leu Lys Gln Thr Ile His Glu Glu Gly Cys Asn Ser Arg Thr
 100 105 110

Ile Ile Asn Arg Phe Cys Tyr Gly Gln Cys Asn Ser Phe Tyr Ile Pro
 115 120 125

Arg His Ile Arg Lys Glu Glu Gly Ser Phe Gln Ser Cys Ser Phe Cys
 130 135 140

Lys Pro Lys Lys Phe Thr Thr Met Met Val Thr Leu Asn Cys Pro Glu
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 <301> Lah, M., Brodnicki, T., Maccarone, P., Nash, A., Stanley, E., and
 Harvey, R.P.
 <302> Human cerberus related gene CER1 maps to chromosome 9
 <303> Genomics
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acc aca cgg cac cag gat ggc cgc cag aat cag agt tct ctt tcc ccc	96
Thr Thr Arg His Gln Asp Gly Arg Gln Asn Gln Ser Ser Leu Ser Pro	
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gta ctc ctg cca agg aat caa aga gag ctt ccc aca ggc aac cat gag	144
Val Leu Leu Pro Arg Asn Gln Arg Glu Leu Pro Thr Gly Asn His Glu	
35 40 45	

gaa gct gag gag aag cca gat ctg ttt gtc gca gtg cca cac ctt gta	192
Glu Ala Glu Glu Lys Pro Asp Leu Phe Val Ala Val Pro His Leu Val	
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gcc acc agc cct gca ggg gaa ggc cag agg cag aga gag aag atg ctg	240
Ala Thr Ser Pro Ala Gly Glu Gly Gln Arg Gln Arg Glu Lys Met Leu	
65 70 75 80	

tcc aga ttt ggc agg ttc tgg aag aag cct gag aga gaa atg cat cca	288
Ser Arg Phe Gly Arg Phe Trp Lys Lys Pro Glu Arg Glu Met His Pro	
85 90 95	

tcc agg gac tca gat agt gag ccc ttc cca cct ggg acc cag tcc ctc 336
 Ser Arg Asp Ser Asp Ser Glu Pro Phe Pro Pro Gly Thr Gln Ser Leu
 100 105 110

atc cag ccg ata gat gga atg aaa atg gag aaa tct cct ctt cgg gaa 384
 Ile Gln Pro Ile Asp Gly Met Lys Met Glu Lys Ser Pro Leu Arg Glu
 115 120 125

gaa gcc aag aaa ttc tgg cac cac ttc atg ttc aga aaa act ccg gct 432
 Glu Ala Lys Lys Phe Trp His His Phe Met Phe Arg Lys Thr Pro Ala
 130 135 140

tct cag ggg gtc atc ttg ccc atc aaa agc cat gaa gta cat tgg gag 480
 Ser Gln Gly Val Ile Leu Pro Ile Lys Ser His Glu Val His Trp Glu
 145 150 155 160

acc tgc agg aca gtg ccc ttc agc cag act ata acc cac gaa ggc tgt 528
 Thr Cys Arg Thr Val Pro Phe Ser Gln Thr Ile Thr His Glu Gly Cys
 165 170 175

gaa aaa gta gtt gtt cag aac aac ctt tgc ttt ggg aaa tgc ggg tct 576
 Glu Lys Val Val Val Gln Asn Asn Leu Cys Phe Gly Lys Cys Gly Ser
 180 185 190

gtt cat ttt cct gga gcc gcg cag cac tcc cat acc tcc tgc tct cac 624
 Val His Phe Pro Gly Ala Ala Gln His Ser His Thr Ser Cys Ser His
 195 200 205

tgt ttg cct gcc aag ttc acc acg atg cac ttg cca ctg aac tgc act 672
 Cys Leu Pro Ala Lys Phe Thr Thr Met His Leu Pro Leu Asn Cys Thr
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gaa ctt tcc tcc gtg atc aag gtg gtg atg ctg gtg gag gag tgc cag 720
 Glu Leu Ser Ser Val Ile Lys Val Val Met Leu Val Glu Glu Cys Gln
 225 230 235 240

tgc aag gtg aag acg gag cat gaa gat gga cac atc cta cat gct ggc 768
 Cys Lys Val Lys Thr Glu His Glu Asp Gly His Ile Leu His Ala Gly
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Val Leu Leu Pro Arg Asn Gln Arg Glu Leu Pro Thr Gly Asn His Glu
 35 40 45

Glu Ala Glu Glu Lys Pro Asp Leu Phe Val Ala Val Pro His Leu Val
 50 55 60

Ala Thr Ser Pro Ala Gly Glu Gly Gln Arg Gln Arg Glu Lys Met Leu
 65 70 75 80

Ser Arg Phe Gly Arg Phe Trp Lys Lys Pro Glu Arg Glu Met His Pro
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Ser Arg Asp Ser Asp Ser Glu Pro Phe Pro Pro Gly Thr Gln Ser Leu
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Ile Gln Pro Ile Asp Gly Met Lys Met Glu Lys Ser Pro Leu Arg Glu
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Glu Ala Lys Lys Phe Trp His His Phe Met Phe Arg Lys Thr Pro Ala
 130 135 140

Ser Gln Gly Val Ile Leu Pro Ile Lys Ser His Glu Val His Trp Glu
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Thr Cys Arg Thr Val Pro Phe Ser Gln Thr Ile Thr His Glu Gly Cys
 165 170 175

Glu Lys Val Val Val Gln Asn Asn Leu Cys Phe Gly Lys Cys Gly Ser
 180 185 190

Val His Phe Pro Gly Ala Ala Gln His Ser His Thr Ser Cys Ser His
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Cys Leu Pro Ala Lys Phe Thr Thr Met His Leu Pro Leu Asn Cys Thr
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Glu Leu Ser Ser Val Ile Lys Val Val Met Leu Val Glu Glu Cys Gln
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Cys Lys Val Lys Thr Glu His Glu Asp Gly His Ile Leu His Ala Gly

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 <301> ten Dijke, P., Yamashita, H., Ichijo, H., Franzen, P., Laiho, M.,
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 <302> Characterization of type I receptors for transforming growth
 factor-beta and activin
 <303> Science
 <304> 264
 <305> 5155
 <306> 101-104
 <307> 1994
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 <301> Ide, H., Katoh, M., Sasaki, H., Yoshida, T., Aoki, K., Nawa, Y.,
 Osada, Y., Sugimura, T., and Terada, M.
 <302> Cloning of human bone morphogenetic protein type IB receptor
 (BMPR-IB) and its expression in prostate cancer in comparison
 with other BMPRs
 <303> Oncogene
 <304> 14
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 <306> 1377-1382
 <307> 1997
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 <301> Ide, H., Saito-Ohara, P., Ohnami, S., Osada, Y., Ikeuchi, T.,
 Yoshida, T., and Terada, M.
 <302> Assignment of the BMPR1A and BMPR1B genes to human chromosome
 10q22.3 and 4q23-->q24 by in situ hybridization and radiation
 hybrid mapping
 <303> Cytogenet. Cell. Genet.
 <304> 81
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 <306> 285-286
 <307> 1998
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<301>  Astrom, A.K., Jin, D., Imamura, T., Roijer, E., Rosenzweig, B.,
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<302>  Chromosomal localization of three human genes encoding bone
        morphogenetic protein receptors
<303>  Mamm. Genome
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gtgaaaggaa aggaagatca tttcatgcct tggtgataaa ggttcagact tctgctgatt      180
cataaccatt tggctctgag ctatgacaag agaggaaaca aaaagttaaa cttacaagcc      240

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Met Leu Leu Arg Ser Ala Gly	
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aaa tta aat gtg ggc acc aag aaa gag gat ggt gag agt aca gcc ccc	342
Lys Leu Asn Val Gly Thr Lys Lys Glu Asp Gly Glu Ser Thr Ala Pro	
10 15 20	
acc ccc cgt cca aag gtc ttg cgt tgt aaa tgc cac cac cat tgt cca	390
Thr Pro Arg Pro Lys Val Leu Arg Cys Lys Cys His His His Cys Pro	
25 30 35	
gaa gac tca gtc aac aat att tgc agc aca gac gga tat tgt ttc acg	438
Glu Asp Ser Val Asn Asn Ile Cys Ser Thr Asp Gly Tyr Cys Phe Thr	
40 45 50 55	
atg ata gaa gag gat gac tct ggg ttg cct gtg gtc act tct ggt tgc	486
Met Ile Glu Glu Asp Asp Ser Gly Leu Pro Val Val Thr Ser Gly Cys	
60 65 70	
cta gga cta gaa ggc tca gat ttt cag tgt cgg gac act ccc att cct	534
Leu Gly Leu Glu Gly Ser Asp Phe Gln Cys Arg Asp Thr Pro Ile Pro	
75 80 85	
cat caa aga aga tca att gaa tgc tgc aca gaa agg aac gaa tgt aat	582
His Gln Arg Arg Ser Ile Glu Cys Cys Thr Glu Arg Asn Glu Cys Asn	
90 95 100	
aaa gac cta cac cct aca ctg cct cca ttg aaa aac aga gat ttt gtt	630
Lys Asp Leu His Pro Thr Leu Pro Pro Leu Lys Asn Arg Asp Phe Val	
105 110 115	
gat gga cct ata cac cac agg gct tta ctt ata tct gtg act gtc tgt	678
Asp Gly Pro Ile His His Arg Ala Leu Leu Ile Ser Val Thr Val Cys	
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Ser Leu Leu Leu Val Leu Ile Ile Leu Phe Cys Tyr Phe Arg Tyr Lys	
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Arg Gln Glu Thr Arg Pro Arg Tyr Ser Ile Gly Leu Glu Gln Asp Glu	
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act tac att cct cct gga gaa tcc ctg aga gac tta att gag cag tct	822
Thr Tyr Ile Pro Pro Gly Glu Ser Leu Arg Asp Leu Ile Glu Gln Ser	
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cag agc tca gga agt gga tca ggc ctc cct ctg ctg gtc caa agg act	870
Gln Ser Ser Gly Ser Gly Ser Gly Leu Pro Leu Leu Val Gln Arg Thr	
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ata gct aag cag att cag atg gtg aaa cag att gga aaa ggt cgc tat	918
Ile Ala Lys Gln Ile Gln Met Val Lys Gln Ile Gly Lys Gly Arg Tyr	
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gca gat atc aaa ggg aca ggg tcc tgg acc cag ttg tac cta atc aca Ala Asp Ile Lys Gly Thr Gly Ser Trp Thr Gln Leu Tyr Leu Ile Thr 265 270 275	1110
gac tat cat gaa aat ggt tcc ctt tat gat tat ctg aag tcc acc acc Asp Tyr His Glu Asn Gly Ser Leu Tyr Asp Tyr Leu Lys Ser Thr Thr 280 285 290 295	1158
cta gac gct aaa tca atg ctg aag tta gcc tac tct tct gtc agt ggc Leu Asp Ala Lys Ser Met Leu Lys Leu Ala Tyr Ser Ser Val Ser Gly 300 305 310	1206
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 Glu Cys Trp Ala His Asn Pro Ala Ser Arg Leu Thr Ala Leu Arg Val
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 50 55 60

Pro Val Val Thr Ser Gly Cys Leu Gly Leu Glu Gly Ser Asp Phe Gln
 65 70 75 80

Cys Arg Asp Thr Pro Ile Pro His Gln Arg Arg Ser Ile Glu Cys Cys
 85 90 95

Thr Glu Arg Asn Glu Cys Asn Lys Asp Leu His Pro Thr Leu Pro Pro
 100 105 110

Leu Lys Asn Arg Asp Phe Val Asp Gly Pro Ile His His Arg Ala Leu
 115 120 125

Leu Ile Ser Val Thr Val Cys Ser Leu Leu Leu Val Leu Ile Ile Leu
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Phe Cys Tyr Phe Arg Tyr Lys Arg Gln Glu Thr Arg Pro Arg Tyr Ser
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Ile Gly Leu Glu Gln Asp Glu Thr Tyr Ile Pro Pro Gly Glu Ser Leu
 165 170 175

Arg Asp Leu Ile Glu Gln Ser Gln Ser Ser Gly Ser Gly Ser Gly Leu
 180 185 190

Pro Leu Leu Val Gln Arg Thr Ile Ala Lys Gln Ile Gln Met Val Lys
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Gln Ile Gly Lys Gly Arg Tyr Gly Glu Val Trp Met Gly Lys Trp Arg
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Gly Glu Lys Val Ala Val Lys Val Phe Phe Thr Thr Glu Glu Ala Ser
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Trp Phe Arg Glu Thr Glu Ile Tyr Gln Thr Val Leu Met Arg His Glu
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Asn Ile Leu Gly Phe Ile Ala Ala Asp Ile Lys Gly Thr Gly Ser Trp
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Thr Gln Leu Tyr Leu Ile Thr Asp Tyr His Glu Asn Gly Ser Leu Tyr
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Ser Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser Lys

325 330 335
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 Tyr Ser Phe Gly Leu Ile Leu Trp Glu Val Ala Arg Arg Cys Val Ser
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 Gly Gly Ile Val Glu Glu Tyr Gln Leu Pro Tyr His Asp Leu Val Pro
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